anti-HER2 antibody or fragment thereof during at least one subsequent cycle, wherein said subsequent cycle comprises daily administration of said therapeutically effective dose of IL-2 or variant thereof on day 1 of said subsequent cycle through day 14 of said subsequent cycle, and administration of said therapeutically effective dose of anti-HER2 antibody on day 1 of said subsequent cycle.

48. (New) The method of claim 42, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of IL-2 or variant thereof an intermediate dose of a pharmaceutical composition comprising IL-2 or variant thereof, wherein said intermediate dose comprises about 12.0 mIU/m^2 IL-2 or variant thereof.

49. (New) The method of claim 47, further comprising intermediate-dose IL-2 pulsing on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of IL-2 or variant thereof an intermediate dose of a pharmaceutical composition comprising IL-2 or variant thereof, wherein said intermediate dose comprises about 12.0 mIU/m^2 IL-2 or variant thereof.

50. (New) The method of claim 47, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle and on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of IL-2 or variant thereof an intermediate dose of a pharmaceutical composition comprising IL-2 or variant thereof, wherein said intermediate dose comprises about 12.0 mIU/m^2 IL-2 or variant thereof.--

REMARKS

Claims 1-11 have been canceled without prejudice to or disclaimer of the subject matter encompassed thereby. Claim 12 has been rewritten in independent form, and claims 16 and 17 have been rewritten in independent form and amended to recite therapeutically effective doses of IL-2 or variant thereof and anti-CD20 antibody or fragment thereof. Accordingly, claims 18-21

has been amended to reflect the recitation of these therapeutically effective doses in claim 17. Claims 14 and 15 have been amended to conform with antecedent basis for recitation of anti-CD20 antibody and fragment thereof. No new matter is added by way of claim amendment.

New claims 22-50 have been added. Claims 22-24 and 26-30 encompass subject matter formerly presented in canceled claims 4-11 and now dependent from amended claim 12, which is rewritten in independent form. Claims 25 and 31 are directed to specific anti-HER2 antibodies within the elected species of anti-CD20 antibody, 4D5, recited in claims new claims 24 and 30. Support for recitation of humanized, chimeric, and human forms of the 4D5 anti-CD20 antibody resides throughout the specification, for example, at pages 21-25, and page 29, lines 12-20. Claims 32-40 are directed to narrow embodiments of claims 12, 16, 17, and 18, and recite the therapeutically effective doses set forth in original claims 13-15. Claim 41 is directed to a multiple IL-2/anti-CD20 antibody dosing regimen incorporating intermediate-dose pulsing in both the introductory and subsequent cycles. Support for this claim resides in the Experimental Protocol described on pages 31 and 32. New claim 42 sets forth claims 17 and 18 rewritten in independent form as a single claim. New claims 43-46 recite specific therapeutically effective doses to be administered in the multiple dosing regimen of claim 42. New claims 47-50 are directed to subsequent cycles of IL-2/anti-CD20 dosing and intermediate-dose pulsing in conjunction with the multiple dosing introductory cycle of claim 42. Support for these new claims resides throughout the specification and in the original claims. No new matter is added by way of presentation of new claims.

Claims 12-50 are now pending in the application. Entry of these claim amendments into the above-referenced application prior to the Examiner's substantive examination on its merits is respectfully requested.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of

this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Commissioner For Patents, Washington, DC 20231.

Lynda-Jo Pixley

Lynda-Jo Pixley

Version with Markings to Show Changes Made:

Please cancel claims 1-11 without prejudice to or disclaimer of the subject matter encompassed thereby.

Please amend claims 12, and 14-21 to read as follows:

12. (Amended) [The method of claim 3,]A method of treating a cancer characterized by overexpression of the HER2 receptor protein in a subject, said method comprising concurrent therapy with an anti-HER2 antibody or fragment thereof and interleukin-2 (IL-2) or variant thereof, wherein said concurrent therapy comprises administering to said subject at least one therapeutically effective dose of IL-2 or variant thereof in combination with a dosing regimen for said anti-HER2 antibody or fragment thereof, wherein said dosing regimen for said anti-HER2 antibody or fragment thereof comprises administering to said subject at least one therapeutically effective dose of said anti-HER2 antibody or fragment thereof, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of IL-2 or variant thereof is in the range from about 0.5 mIU/m^2 to about 4.0 mIU/m^2.

14. (Amended) The method of claim 13, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 3.0 mg/kg to about 8.0 mg/kg and wherein said therapeutically effective dose of IL-2 or variant thereof is in the range from about 0.8 mIU/m^2 to about 1.5 mIU/m^2.

15. Amended) The method of claim 14, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is about 4.0 mg/m^2 and wherein said therapeutically effective dose of IL-2 or variant thereof is about 1.0 mIU/m^2.

16. (Amended) [The method of claim 3] A method of treating a cancer characterized by overexpression of the HER2 receptor protein in a subject, said method comprising concurrent

therapy with an anti-HER2 antibody or fragment thereof and interleukin-2 (IL-2) or variant thereof, wherein said concurrent therapy comprises a first administration of [said]a therapeutically effective dose of IL-2 or variant thereof on day 1 of a treatment period followed by a first administration of [said]a therapeutically effective dose of anti-HER2 antibody or fragment thereof within 6 days of said first administration of said [anti-HER2 antibody or fragment thereof]therapeutically effective dose of IL-2 or variant thereof to said subject, wherein said therapeutically effective dose of anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of IL-2 or variant thereof is in the range from about 0.5 mIU/m^2 to about 4.0 mIU/m^2.

17. (Amended) [The method of claim 3] A method of treating a cancer characterized by overexpression of the HER2 receptor protein in a subject, said method comprising concurrent therapy with an anti-HER2 antibody or fragment thereof and interleukin-2 (IL-2) or variant thereof, wherein said concurrent therapy comprises multiple dosing of [said]a therapeutically effective dose of anti-HER2 antibody or fragment thereof and [said]a therapeutically effective dose of IL-2 or variant thereof, wherein said therapeutically effective dose of anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of IL-2 or variant thereof is in the range from about 0.5 mIU/m^2 to about 4.0 mIU/m^2.

18. (Amended) The method of claim 17, wherein said multiple dosing comprises administering to said subject said therapeutically effective dose of IL-2 or variant thereof and said therapeutically effective dose of anti-HER2 antibody or fragment thereof during an introductory cycle, wherein said introductory cycle comprises [administering a daily dose of]daily administration of said therapeutically effective dose of IL-2 or variant thereof on day 1 of said introductory cycle through day 20 of said introductory cycle, and [administering] a single administration of said therapeutically effective dose of [said]anti-HER2 antibody or fragment thereof on day 7 of said introductory cycle.

19. (Amended) The method of claim 18, further comprising administering said therapeutically effective dose of IL-2 or variant thereof and said therapeutically effective dose of anti-HER2 antibody or fragment thereof during at least one subsequent cycle, wherein said subsequent cycle comprises [administering a daily]daily administration of said therapeutically effective dose of IL-2 or variant thereof on day 1 of said subsequent cycle through day 14 of said subsequent cycle, and [administering]administration of said therapeutically effective dose of [said]anti-HER2 antibody or fragment thereof on day 1 of said subsequent cycle.

20. (Amended) The method of claim 18, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of [said]IL-2 or variant thereof an intermediate dose of a pharmaceutical composition comprising IL-2 or variant thereof, wherein said intermediate dose comprises about 12.0 mIU/m^2 IL-2 or variant thereof.

21. (Amended) The method of claim 19, further comprising intermediate-dose IL-2 pulsing on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of [said]IL-2 or variant thereof an intermediate dose of a pharmaceutical composition comprising IL-2 or variant thereof, wherein said intermediate dose comprises about 12.0 mIU/m^2 IL-2 or variant thereof.